Remarks

Upon entry of this amendment, claims 21-25, 28-44, 47-51, 54-78, 80-84, 87-103, 106-110, 113-119, 122-137, and 139-198 will be pending in the above-captioned application. Claims 19, 26-27, 52-53, 61-62, 85-86, 111-112, and 120-121 have been canceled without prejudice or disclaimer. Claims 45-46, 79, 104-105 and 138 have been withdrawn from consideration by the Examiner.

Claims 21, 47, 56, 80, 106, and 115 have been amended to delete subparts (e) and (f) of each claim directed to a protein consisting of a portion of SEQ ID NO:2 or of the polypeptide encoded by the cDNA contained in ATCC Deposit No. 209023, wherein the portion comprises at least 30 or 50 contiguous amino acid residues. New claims 184-198 have been added and correspond in part to the canceled subject matter of claims 21, 47, 56, 80, 106, and 115, subparts (e) and (f). New claims 184-198 are directed to an isolated antibody or fragment thereof that specifically binds or has been obtained from an animal that has been immunized with a protein consisting of a portion of SEQ ID NO:2 or of the polypeptide encoded by the cDNA contained in ATCC Deposit No. 209023, wherein the portion is at least 30 or 50 contiguous amino acid residues in length. Support for new claims 184-198 can be found in the specification as filed, for example, at page 65, paragraph 148 to page 66, paragraph 152; and at page 84, paragraph 203 to page 92, paragraph 225.

Claims 34, 68, 93, 127,162, and 178 have been amended to delete the recitations of "a luminescent label" and "a bioluminescent label". In addition, these claims have been amended to include "a chemiluminescent label". Support for this amendment can be found in the specification as filed, for example, at page 205, paragraph 633 to page 206, paragraph 636.

Claims 41, 75, 100, and 134 have been amended to replace the term "portion" with "fragment" as suggested by the Examiner. Claim 139 has been amended to recite "An isolated antibody or fragment thereof that specifically binds a t-PALP protein purified from a cell culture wherein said t-PALP protein is expressed by cells comprising a polynucleotide encoding amino acids 1 to 242 of SEQ ID NO:2." Support for this amendment can be found in the specification as filed, for example, at page 88, paragraph 217 to page 89, paragraph 220.

The first paragraph of the specification has been amended to reflect the current status of parent U.S. Application Nos. 09/411,977 and 09/084,491, as requested by the

Examiner. In addition, this paragraph has been amended to reflect the current format for a benefit claim.

Accordingly, no new matter has been introduced and entry of this amendment is respectfully solicited.

I. Withdrawn Claims

The Examiner has withdrawn claims 45-46, 79, 104-105, and 138 from further consideration under 37 C.F.R. § 1.142(b) as allegedly being drawn to a nonelected invention. *See* Paper No. 6, page 2, paragraph 3. Applicants note that claims 45-46, 79, 104-105, and 138 are method of use claims which depend from (and thus contain all of the limitations of) independent claims 21, 56, 80, and 115, respectively. Accordingly, pursuant to M.P.E.P. § 821.04 at 800-63, Applicants respectfully request the Examiner to rejoin claims 45-46, 79, 104-105, and 138 upon the allowance of independent claims 21, 56, 80, and 115.

II. Objections to the Specification

A. Figure 2

The Examiner has objected to the specification due to alleged discrepancy between the disclosure of the specification and Figure 2. In particular, the Examiner states on page 2, paragraph 7 of Paper No. 6 that:

> Figure 2 shows an alignment of t-PALP and human t-PA. SEQ ID NO:2 consisting of 263 amino acids is aligned with residues 191-516 of t-PA. On page 8, line 9, the t-PA sequence is referred to as SEQ ID NO:3. SEQ ID NO:3 has 372 amino acids. Residues 191-516 of t-PA on Figure 2 correspond to residues 1-326 of SEQ ID NO:3. Appropriate correction is required.

Applicants respectfully disagree and point out that the specification, for example, at page 9, paragraph 29, equates amino acid residues 191 to 516 of t-PA as depicted in Figure 2 with amino acid residues 1-325 of SEQ ID NO:3. Thus, Applicants believe that no further correction is required and respectfully request the Examiner to reconsider and withdraw this objection.

B. Claim 19

The Examiner has further objected to claim 19 for being dependent on canceled claim 17. *See* Paper No. 6, page 3, paragraph 8. Applicants have canceled claim 19, thus rendering the objection moot. Applicants respectfully request the Examiner to reconsider and withdraw this objection.

III. Indefiniteness Rejections

A. Claims 41, 75, 100, and 134

The Examiner has rejected claims 41, 75, 100, and 134 under 35 U.S.C. § 112, second paragraph for alleged indefiniteness. In particular, the Examiner asserts that the recitation of "the antibody of portion thereof" in the rejected claims lacks antecedent basis. *See* Paper No. 6, page 3, paragraph 11A.

In response, Applicants have amended claims 41, 75, 100, and 134 to replace the term "portion" with "fragment", thus rendering the rejection moot. Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of claims 41, 75, 100, and 134 under 35 U.S.C. § 112, second paragraph.

B. Claim 139

The Examiner has also rejected claim 139 under 35 U.S.C. § 112, second paragraph for alleged indefiniteness. In particular, the Examiner asserts that the term "operably associated" is indefinite and ambiguous. *See* Paper No. 6, page 3, paragraph 11B.

Applicants respectfully disagree and assert that the language of claim 139 clearly sets forth the metes and bounds of the subject matter claimed as originally presented. However, Applicants have amended the claim such that the isolated antibody or fragment thereof "specifically binds a t-PALP protein purified from a cell culture wherein said t-PALP protein is expressed by cells comprising a polynucleotide encoding amino acids 1 to 242 of SEQ ID NO:2." Thus, the objectionable language has been deleted. Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of claim 139 under 35 U.S.C. § 112, second paragraph.

IV. New Matter Rejection

The Examiner has rejected claims 34, 93, 127, 162, and 178 under 35 U.S.C. § 112, first paragraph as allegedly containing new matter. In particular, the Examiner alleges that

> Examiner noticed that page 113 (¶307) discloses enzyme labels such as glucose oxidase and radioisotopes, however, the specification does not provide clear support of "a luminescent label" and "a bioluminescent label". The instant claims now recite limitations which were not clearly disclosed in the specification and claims as originally filed.

See Paper No. 6, pages 3-4, paragraph 13.

Applicants respectfully disagree and maintain that these claims are fully supported by the specification. However, Applicants have amended the claims at issue to delete the recitations of "a luminescent label" and "a bioluminescent label," thus removing the language objected to be the Examiner. In addition, these claims have been amended to include "a chemiluminescent label". Support for this amendment can be found in the specification as filed, for example, at page 205, paragraph 633 to page 206, paragraph 636. Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of claim 34, 93, 127, 162, and 178 under 35 U.S.C. § 112, first paragraph.

V. Enablement Rejection

The Examiner has rejected claims 19, 21-44, 47-78, 80-103, and 106-137 under U.S.C. § 112, first paragraph for alleged lack of enablement. In particular, the Examiner asserts that

> ...the specification, while being enabling for an antibody or antigen binding fragment thereof that specifically binds amino acids -20 to 242, 1 to 242, 4 to 63, 64 to 242, 1 to 10, 14 to 23, 50 to 60, 70 to 86, 98 to 107, 117 to 126, 134 to 146, 172 to 182, 185 to 194, 206 to 216 and 22 to 231 of SEQ ID NO:2, does not reasonably provide enablement for any isolated antibody that binds specifically to any t-PALP polypeptide "comprising" an amino acid sequence at least 95% identical to amino acids -20 to 242, 1 to 242, 4 to 63, 64 to 242 of SEQ ID NO:2 or as encoded by cDNA clone contained in the ATCC Deposit No. 209023 in canceled base 17, an isolated antibody or fragment thereof that specifically binds to a protein consisting of a portion of SEQ ID NO:2, wherein said portion comprises at least 30 or 50 contiguous amino acid residues of SEQ ID NO:2 in claims 21(e and f), 47 (e and f), 56 (e and f), 80 (e and f), 106 (e and f) and 115 (e and f).

Paper No. 6, page 4, paragraph 15 (emphasis in original).

Applicants respectfully disagree and traverse.

Preliminarily, Applicants note that claim 19 has been canceled, thereby making the rejection of this claim moot. Applicants further note that none of the pending (or previously pending) claims contain the phrase "95% identical" to which the Examiner objected. Thus, the Examiner's arguments based on percent identity are also moot. Accordingly, Applicants will address the Examiner's remaining argument regarding enablement of an antibody or fragment thereof that specifically binds a protein consisting of a portion of SEQ ID NO:2, wherein said portion comprises at least 30 or 50 contiguous amino acid residues of SEQ ID NO:2 or of the polypeptide encoded by the cDNA contained in ATCC Deposit No. 209023.

Applicants have amended claims 21, 47, 56, 80, 106, and 115 to delete the subject matter directed to 30 and 50 contiguous amino acids. Thus, the subject matter of amended claims 21, 47, 56, 80, 106, and 115 are directed to antibodies or fragments thereof that specifically bind a protein consisting of specific amino acid residues of SEQ ID NO:2 or encoded by the cDNA contained in ATCC Deposit No. 209023, including amino acid residues -20 to 242, 1 to 242, 4 to 63, and 64 to 242. As noted by the Examiner on page 4, paragraph 15 of Paper No. 6, the specification is fully enabled for the subject matter encompassed by amended claims 21, 47, 56, 80, 106, and 115, and thus these claims should be allowable.

In addition, new claims 184-198 were added and correspond in part to the canceled subject matter of claims 21, 47, 56, 80, 106, and 115 subparts (e) and (f). These claims are directed to an antibody or fragment thereof that specifically binds to a protein consisting of a portion of SEQ ID NO:2 or the polypeptide encoded by the cDNA contained in ATCC Deposit No. 209023, wherein the portion is at least 30 or 50 contiguous amino acids in length. Thus, contrary to the Examiner's argument and for the reasons set forth below, Applicants contend that the pending claims are fully enabled by the instant application.

Applicants note that the underlying basis for the Examiner's rejection on page 5 of Paper No. 6 is the assumption that the pending claims encompass variants with a different amino acid sequence from SEQ ID NO:2 due to alleged percent identity language and "comprising" language in relation to 30 and 50 contiguous amino acid residues. However, as noted above, the pending claims do not recite any percent identity language. Moreover, new claims 184-198 do not contain the open-ended term "comprising", instead recite that

the antibody or fragment thereof specifically binds a protein consisting of a portion of the t-PALP protein in which the portion must be at least 30 or 50 contiguous amino acids in length.

Thus, the antibodies encompassed by the pending claims are only required to bind the amino acid sequence of SEQ ID NO:2 or the polypeptide encoded by the cDNA contained in the ATCC deposit and fragments thereof. Therefore, the Examiner's argument that changes in the amino acid sequence by, for example, amino acid substitution, might change the binding specificity of the antibody is moot. All that is required for the pending claims to be fully enabled is that the specification teaches the skilled artisan to make fragments of the t-PALP amino acid sequence, generate antibodies, and then screen these antibodies to determine those that specifically bind to the t-PALP amino acid sequence or a fragment thereof.

Applicants contend that the specification clearly teaches one of skill in the art how to make and isolate polypeptides of SEQ ID NO:2 or encoded by the cDNA contained in ATCC Deposit 209023 which are at least 30 or 50 contiguous amino acids in length. *See* specification, for example, at page 46, paragraph 103 to page 47, paragraph 104; at page 48, paragraph 107 to page 51, paragraph 117; at page 52, paragraph 119 to page 60, paragraph 136; at page 60, paragraph 138 to page 64, paragraph 145; at page 65, paragraph 148 to page 66, paragraph 152. In addition, the specification teaches, for example, at page 84, paragraph 203 to page 92, paragraph 225, how to make, isolate, and screen for antibodies that specifically bind t-PALP polypeptides, including fragments. Thus, the specification clearly teaches the skilled artisan how to make and use the claimed invention.

For all of the above reasons, Applicants assert that the specification is fully enabling for the subject matter encompassed by the pending claims. Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection under 35 U.S.C. § 112, first paragraph for lack of enablement.

VI. Written Description Rejection

The Examiner has rejected claims 19, 21-44, 47-78, 80-103, and 106-137 under 35 U.S.C. § 112, first paragraph for alleged lack of written description. In particular, the Examiner contends that:

> Applicant is in possession of an antibody or antigen binding fragment thereof that specifically binds amino acids -20 to 242, 1 to 242, 4 to 63, 64

to 242, 1 to 10, 14 to 23, 50 to 60, 70 to 86, 98 to 107, 117 to 126, 134 to 146, 172 to 182, 185 to 194, 206 to 216 and 22 to 231 of SEQ ID NO:2. Applicant is not in possession of any isolated antibody that binds specifically to any t-PALP polypeptide "comprising" an amino acid sequence at least 95% identical to amino acids -20 to 242, 1 to 242, 4 to 63, 64 to 242 of SEQ ID NO:2 or as encoded by cDNA clone contained in ATCC Deposit No. 209023 in canceled base 17, an isolated antibody or fragment thereof that specifically binds to a protein consisting of a portion of SEQ ID NO:2, wherein said portion comprises at least 30 or 50 contiguous amino acid residues of SEQ ID NO:2 in claims 21 (e and f), 47 (e and f), 56 (e and f), 80 (e and f), 106 (e and f), and 115 (e and f).

See Paper No. 6, page 6, paragraph 16.

Applicants respectfully disagree and traverse. As stated above, Applicants have canceled claim 19, thus making the rejection of this claim moot. Applicants further reiterate that none of the pending (or previously pending) claims contain the term "95% identical" to which the Examiner objected. Thus, the Examiner's arguments based on percent identity are also moot. Accordingly, Applicants will address the Examiner's remaining argument regarding written description of an antibody or fragment thereof that specifically binds a protein consisting of a portion of SEQ ID NO:2, wherein said portion comprises at least 30 or 50 contiguous amino acid residues of SEQ ID NO:2 or of the polypeptide encoded by the cDNA contained in ATCC Deposit No. 209023.

Applicants have amended claims 21, 47, 56, 80, 106, and 115 to delete the subject matter directed to 30 and 50 contiguous amino acids. Thus, the subject matter of amended claims 21, 47, 56, 80, 106, and 115 are directed to antibodies or fragments thereof that specifically bind a protein consisting of specific amino acid residues of SEQ ID NO:2 or encoded by the cDNA contained in ATCC Deposit No. 209023, including amino acid residues -20 to 242, 1 to 242, 4 to 63, and 64 to 242. As noted by the Examiner on page 6, paragraph 16 of Paper No. 6, Applicants are in full possession of the subject matter encompassed by amended claims 21, 47, 56, 80, 106, and 115.

In addition, new claims 184-198 were added and correspond in part to the deleted subject matter of claims 21, 47, 56, 80, 106, and 115 subparts (e) and (f). These claims are directed to an antibody or fragment thereof the specifically binds to a protein consisting of a portion of SEQ ID NO:2 or the polypeptide encoded by the cDNA contained in ATCC Deposit No. 209023, wherein the portion is at least 30 or 50 contiguous amino acids in length. Thus, contrary to the Examiner's argument and for the reasons set forth below, Applicants contend that the pending claims are fully described in the instant specification.

The test for the written description requirement is whether one skilled in the art could reasonably conclude that the inventor has possession of the claimed invention in the specification as filed. *See* M.P.E.P. § 2163(I) at 2100-15, and *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). In particular, written description is satisfied if the specification allows the skilled artisan "to visualize or recognize the identity of the members of the genus." *See* Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicants submit that the specification provides ample written description to enable one of skill in the art to visualize or recognize the identity of the members of the claimed genus. For example, the specification provides the skilled artisan with the detailed structure of the polypeptides of the invention, *e.g.*, the amino acid sequence of SEQ ID NO:2. *See*, for example, specification at page 4, paragraph 10; at page 4, paragraph 12; page 9, paragraphs 27-28; at page 17, paragraph 36 and at Figures 1A-1C.

In addition to the amino acid sequence common to the polypeptides of the claimed invention (e.g., SEQ ID NO:2), the specification further provides ample disclosure of other relevant characteristics of the claimed polypeptides. The specification further provides a detailed analysis of the structural attributes of the polypeptides of SEQ ID NO:2, including N-terminal and C-terminal deletion mutants and antigenic peptides, many of which are encompassed within the scope of the claims. *See*, for example, specification at page 48, paragraph 107 to page 64, paragraph 145. Moreover, the specification provides specific fragments of SEQ ID NO:2 which are at least 30 or 50 contiguous amino acids in lengths, for example, 4 to 63, 64 to 242, and 22 to 231, all of which fall within the scope of the claims at issue. *See* specification, for example, at page 58, paragraph 130; and at page 60, paragraph 139.

The specification also provides a detailed analysis of the functional attributes of polypeptides of SEQ ID NO:2, such as, for example, antigenic index. *See* specification, for example, at page 10, paragraphs 30-31; at page 67, paragraph 157 to page 68, paragraph 159; at Table 1; and at Figure 3. In particular, the specification discloses specific antigenic regions and epitope-bearing portions of the polypeptides of SEQ ID NO:2. *See* specification, for example, at page 10, paragraphs 30-31; page 77, paragraph 181 to page 79, paragraph 189; at Table 1; and at Figure 3. The specification further antibodies that specifically bind a polypeptide of SEQ ID NO:2. *See* specification, for example, at page 84, paragraph 203 to page 91, paragraph 223.

Accordingly, one skilled in the art, enlightened by teachings of the present application, could readily envision the polypeptide sequences that comprise the specified polypeptides of SEQ ID NO:2 which are at least 30 or 50 contiguous amino acids in length. Indeed, nothing more than what is described in the specification would be required for the skilled artisan to identify every single one of the polypeptides of SEQ ID NO:2 that are at least 30 or 50 amino acids in length. Moreover, the skilled artisan can then readily determine using techniques well-known within the art whether the antibody or fragment thereof specifically binds such portions of SEQ ID NO:2. Clearly, such knowledge is well within what is expected of the skilled artisan.

Thus, the instant claims clearly distinguish the boundaries of each claimed genus and identify all of the members of each genus. Accordingly, one skilled in the art would reasonably conclude that Applicants had possession of the polypeptides encompassed by the rejected claims, upon reading the present application as filed.

Accordingly, from reading the specification, the skilled person would immediately recognize that, at the time the specification was filed, the Applicants had "invented what is claimed" (*Vas-Cath*, 935 F.2d at 1563); namely, a genus of antibodies or portions thereof that specifically bind to a protein consisting of a portion of SEQ ID NO:2, wherein said portion is at least 30 or 50 contiguous amino acid residues in length. Therefore, the specification contains an adequate written description of the claimed antibodies.

For all of the above reasons, Applicants respectfully assert that the specification conveys with reasonable clarity that Applicants were in possession of the claimed invention. Therefore, Applicants submit that the pending claims fully meet the written description requirements of 35 U.S.C. § 112, first paragraph, and respectfully request that the Examiner's rejection of the claim 183-200 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Conclusion

Applicants respectfully request that the above-made remarks and amendments be entered and made of record in the file history of the instant application. In view of the foregoing remarks, Applicants believe that this application is now in condition for allowance, and an early notice to that effect is urged. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicant would expedite the allowance of this application. If there are any fees due in connection with the

filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136, such an extension is requested and the fee should also be charged to our Deposit Account.

Dated: August 4, 2003

Respectfully submitted,

By _____

Mark J. Hyman
Registration No.: 46,789
HUMAN GENOME SCIENCES, INC.
9410 Key West Avenue
Rockville, Maryland 20850
(240) 314-1224

MMW/MJH/KC/lcc